AMENDMENTS TO THE SPECIFICATION

Please amend the Specification as follows. Additions are shown underlined, and deletions are shown in ~~stricken through~~.

Please replace paragraph **[0086]** with the following amended paragraph:

[0086] In one embodiment of the invention, the apparatus and/or method for treating cardiovascular disease includes one or more signal processors. In one embodiment, the signal processor determines a processor output that is indicative of an appropriate therapeutic treatment in response to the pressure-indicative signal provided by the sensor. The processor output is provided to a signaling device, which provides an appropriate treatment signal to the medical patient. The term "processor output" as used herein shall be given its ordinary meaning and shall also mean output from a signal processor and/or input to a signaling device, and shall include, but not be limited to, signals, including analog, digital, and/or optical signals, data, code, and/or text. The treatment signal may be provided by, for example, vibrating a signaling device located within the implantable housing. Alternatively, the treatment signal may be generated within the implantable housing and transmitted to a signaling device located external to the patient, such as a personal digital ~~recorder~~ assistant (PDA). In another embodiment, the sensor signal is transmitted to an external device, such as, for example, a PDA, which includes a processor and signaling device to generate a processor output and provide a treatment signal to the patient. These and other embodiments are described in greater detail below.

Please replace paragraph **[0087]** with the following amended paragraph:

[0087] In one embodiment of the invention, the apparatus and/or method for treating cardiovascular disease includes one or more signaling devices. In one embodiment, the signaling device includes a buzzer, an alarm, a display, a computer, a telephone, or a PDA, such as a PALM PILOT™ (Palm Computing, Inc.)~~Pilot~~, or a HANDSPRING VISOR® (Handspring, Inc.) ~~Visor~~. The signaling device may be operable to generate at least two treatment signals distinguishable from one another by the patient. In one embodiment, each signal is indicative of a different therapeutic treatment. The treatment signal may be an electrical pulse, a vibration, a noise, audio or visual data, including, but not limited to, instructions on a display screen or light

emitting diodes. In one embodiment, the at least two treatment signals may include two numerical values or designations, a numerical value and an electrical pulse or vibration, multiple vibrations of varying amplitudes, durations, or frequencies, or any combination of two or more of any of the treatment signals described herein. In one embodiment, the signaling device is a PDA that displays an instruction, such as "take medication," "rest," or "call Doctor". These and other embodiments are described in greater detail below.

Please replace paragraph **[0090]** with the following amended paragraph:

[0090] As shown in **FIG. 3**, in one embodiment housing 7 includes a power supply 153, a CRM system 159, and a signal processing and patient signaling modules 157. The CRM system 159 is configured to provide an electrical stimulus, such as a pacing signal, to the patient's heart, and receive a sensor signal from implanted sensors (not shown). In one embodiment, the CRM system 159 is configured to control a defibrillator. The signal processing module 157 is coupled to at least one sensor that provides a signal indicative of the fluid pressure within the left atrium of the heart. The signal processing module 157 may also be configured to control ~~a~~ distally implanted CRM components, or a sensor package or module, as described in greater detail herein.

Please replace paragraph **[0097]** with the following amended paragraph:

[0097] The patient advisory module 6 may include an RF unit 168 and a barometer 112 for measuring the reference atmospheric pressure. In one embodiment, the RF unit 168 and barometer are located within the telemetry module 164, although they can be integrated with the processing unit 166 as well. The signal processing unit can be used to analyze physiologic signals and to determine physiologic parameters. The patient advisory module 166 may also include data storage, and a sub-module that contains the physician's instructions to the patient for therapy and how to alter therapy based on changes in physiologic parameters. The parameter based physician's instructions are typically referred to as "the dynamic prescription," or DynamicRx™ (Savacor, Inc.). The instructions are communicated to the patient via the signaling module 166, or another module. The patient advisory module 166 is located externally and used by the patient or his direct caregiver. It may be part of system integrated with a

personal digital assistant, a cell phone, or a personal computer, or as a Stand-Alone device. In one embodiment, the external patient advisory module comprises an external telemetry device, a signal processing apparatus, and a patient signaling device. In one embodiment, the patient advisory module is operable to obtain the sensor signal from the implantable sensor by telemetry through the patient's skin; obtain the atmospheric pressure from the barometer; and adjust the sensor signal indicative of a fluid pressure based at least in part upon the atmospheric pressure obtained by the barometer so that the adjusted sensor signal indicates the fluid pressure within the left atrium of the heart relative to the atmospheric pressure.

Please replace paragraph **[0112]** with the following amended paragraph:

[0112] In one embodiment, such as that illustrated in **FIG. 8**, an implantable device is implanted percutaneously in the patient by approaching the left atrium 36 through the right atrium 30, penetrating the patient's atrial septum 41 and positioning one or more physiological sensors 15 in the atrial septum 41, on the septal wall of the left atrium 36, or inside the patient's left atrium 36. **FIG. 8** shows an embodiment in which a sensor package 15 is deployed across the atrial septum 41. The sensor lead 10 is coupled to a physiological sensor or sensors 15 and anchoring apparatus at the lead 10 distal end 17. The anchoring apparatus includes a distal foldable spring anchor 68 that expands in diameter upon release and is located at or near the distal tip of the sensor 15, and a proximal foldable spring anchor 70. The distal and proximal anchors 68, 70 are sufficiently close together that when deployed the two anchors 68, 70 sandwich the intra-atrial septum 41 between them, thus fixing the sensor/lead system to the septal wall. The intra-atrial septum 41 is typically between about 1 and about 10 mm thick. In one embodiment, the anchors 68, 70 are made of a highly elastic biocompatible metal alloy such as superelastic nitinol. The lead 10 may contain a lumen that exits the lead 10 at its proximal end. A stiffening or bending stylet can be insert in the lumen to aid in passage of the sensor(s) and lead 15, 10. After a transseptal catheterization has been performed, a sheath/dilator system of diameter sufficient to allow passage of the sensor/lead system is placed from a percutaneous insertion site over a guidewire until the distal end of a sheath 67 is in the left atrium 36. Left atrial position can be confirmed under fluoroscopy by contrast injection, or by the pressure waveform obtained when the sheath 67 is connected to a pressure transducer. To aid the

procedure, the sheath 67 may include a proximal hemostasis valve to minimize air entrainment during device insertion. A side port with a stopcock is useful to aspirate any remaining air and to inject radiographic contrast material. Additionally, later sheath 67 removal may be facilitated by using a "peel-away" type of sheath. These features of vascular sheaths are commercially available and well know to those familiar with the art. With the spring anchors 68, 70 folded and forming a system with minimal diameter, the system is loaded into the sheath 67 and advanced until the distal spring 68 just exits the sheath 67 in the left atrium 36 and is thus deployed to its sprung diameter. The sheath 67 is carefully withdrawn without deploying the proximal anchor 70 and the sheath 67 and sensor/lead system are withdrawn as a unit while contrast is injected through the sheath 67 around the sensor lead until contrast is visible in the right atrium 30. The proximal sheath 67 is further withdrawn, allowing the proximal anchor 70 to spring to its unloaded larger diameter, thus fixing the distal portion of the sensor lead to the septum 41.

Please replace paragraph **[0115]** with the following amended paragraph:

[0115] In other embodiments, such as those shown in **FIG. 12** and **FIG. 14**, a first lead component 53 includes an anchoring apparatus, for example, a helical screw 57, which is advanced to the atrial septum 41. The anchoring apparatus is deployed to anchor the first lead component 53 into the patient's atrial septum 41. A second lead component 60 includes a physiological sensor, for example, a pressure transducer 62, which is advanced along the first lead component 53 until the second lead component 60 is in a position such that the physiological sensor is positioned within the patient's left atrium 36.

Please replace paragraph **[0141]** with the following amended paragraph:

[0141] In one embodiment, the sensor package includes a titanium cylindrical housing that is closed at one end by titanium foil membrane. In one embodiment, the foil membrane is between about 0.001 to 0.003 inches, between about 0.003 inches and about 0.005 inches, or less than 0.001 inches thick. In another embodiment, the foil membrane is between about 25 microns to about 50 microns thick, and about 0.08 to 0.10 inches (about 2.0 to 2.5 mm) in diameter. Foil diaphragms of this type have relatively low compliance, meaning that they exhibit relatively little strain, or displacement, in response to changes in pressure. For example,

in one embodiment, a 2.5 mm diameter by 50-micron thick titanium foil diaphragm has a displacement at its center of only about 4.3 ~~microns~~ nanometers per mm Hg pressure change. Higher compliance is a disadvantage for implantable pressure sensors because tissue overgrowth can limit the relatively larger motion of a high compliance diaphragm, causing errors in the sensed pressure reading.

Please replace paragraph **[0198]** with the following amended paragraph:

[0198] According to one embodiment of the invention, one or more physiological sensors is implanted within the body, the signal processing apparatus and the patient signaling device are located outside the body, and the signal indicative of a physiological parameter is communicated by wireless telemetry through the patient's skin. In one embodiment, an external telemetry system is combined with the signal processing apparatus and the patient signaling device. In one embodiment, a hand-held personal data assistant (PDA), such as the PALM PILOT™ (Palm Computing, Inc.) ~~Pilot~~ and/or HANDSPRING VISOR® (Handspring, Inc.), ~~Visor~~ is used for the signal processing and patient signaling apparatus. In one embodiment, patient signaling is accomplished using sound, text, and/or images.

Please replace paragraph **[0204]** with the following amended paragraph:

[0204] It will also be known to those skilled in the art that pacing multichamber sites in appropriate sequence in addition to the atria, such as the right ventricle and the lateral wall of the left ventricle in combination, or the lateral wall of the left ventricle alone, has specific advantages for some patients with congestive heart failure. **FIG. 20** illustrates one embodiment of the present invention in which a sensor package 15 at the end of flexible lead 10 is implanted across the atrial septum 41 of a patient's heart 33. The sensor package 15 measures the left atrial pressure and also serves as the atrial septal pacing electrode 215 of a CRM device, which may be located within an implanted housing 7. A second flexible lead 160 is placed via the right atrium 30 into the right ventricle 37. Each lead is shown with an indifferent electrode 14 proximal to its respective distal electrode 215, although those skilled in the art will recognize one of these could be eliminated. The housing 7 contains the CRM device (not shown), which in one embodiment includes a battery and electrical circuitry for pacing the heart 33, and components of a

physiological monitoring system. It will be clear to the skilled artisan that a variety of configurations may be used to combine the CRM and physiological monitoring functions of such a combined device, examples of which are described below.

Please replace paragraph **[0221]** with the following amended paragraph:

[0221] In one embodiment, the surface area of the pacing electrode 204 is reduced by coating selected areas of the metallic distal segment 210 with an insulating material. In one embodiment, the insulating material is a tenacious thin coating such as, for example, parylene. One or more selected small areas may be masked off prior to coating to provide for one or more electrically conducting pacing electrodes 204. Referring now to **FIG. 23**, in ~~In~~ one embodiment, the pacing electrode 204 includes an annular region ~~212~~222. In another embodiment, the pacing electrodes 204 include areas on the distal anchor members 214 such that the pacing current is applied preferentially to the left atrial wall of the septum. In one embodiment, the pacing electrodes 204 include metallic electrodes fastened to tips of one or more of the distal anchor members 214. In one embodiment, the metallic tip electrodes are made of tantalum, which has the desirable property that it can be made as a porous, high surface area material. It will be familiar to the skilled artisan that such materials reduce contact impedance with tissue. Tantalum has the additional property of high x-ray density, which allows the anchor tips to be visualized under fluoroscopy for verifying the positioning and deployment of the anchor 214.

Please replace paragraph **[0224]** with the following amended paragraph:

[0224] In one embodiment of the present invention, a defibrillator and an implantable heart monitor (such as described above with reference to **FIG. 1** through **FIG. 5**) are combined to provide the following functionality via an essentially standard pacing/defibrillator lead with only two conductors: (1) provide power to a physiologically optimized dosimeter (POD) measurement module(s); (2) provide signaling for atrial and/or ventricular pacing and sensing, (3) provide for atrial and/or ventricular defibrillation through a third lead attached to a defibrillation electrode; (4) provide for programming of the physiological sensor package; and (5) provide measurement data from the physiological sensor package(s) to the

monitor/defibrillator housing for storage and recovery by, e.g., a doctor or the patient via the patient signaling module.

Please replace paragraph **[0239]** with the following amended paragraph:

[0239] In one embodiment, in the CRM mode, the sensor lead 318 is attached to a CRM device 306 that provides a power pulse at a fixed frame rate, a pace trigger signal, and apparatus for changing memory registers in the POD. The power pulse is rectified to provide DC power for the POD electronics. The reflected impedance shorting FET used in the Stand-Alone mode is disabled at power up and in CRM mode. A frame clock detector 308 is employed to obtain the frame clock that is input to a DPLL 310 (digital phase lock loop). The DPLL 310, by way of example, includes or is coupled to an oscillator 311 with electronic frequency adjustment with its output used for operation and timing for the POD electronics. This clock is fed into a divide by N counter (or bit counter) 312 through a clock select switch 314. The output of the bit counter 312 ~~whose output~~ is coupled to the other input of the DPLL 310, ~~to an up/down counter 312~~ whose output is connected to the frequency adjustment of the oscillator 311 ~~coupled to the DPLL 310~~. The divide by N counter 314 output may be coupled directly to the up/down counter 312 (or bit counter 312), or may be coupled to a clock select module 314 which is coupled to the bit counter 312, as shown in FIG. 26B. This provides for an internal clock, which is N times the frame clock and is synchronized to the frame clock. In another embodiment, an analog PLL is used instead of a digital PLL. The DPLL 310 also provides a signal to indicate the mode of operation (the frequency discrimination method). If the DPLL 310 is locked at its limit (no sync), then Stand-Alone operation is indicated. In the CRM mode, the CRM device 306 goes to high impedance between power pulses during the upload period, thereby allowing the POD to send sensor output(s) and a pacing sense-detect signal to the CRM device 306.

Please replace paragraph **[0258]** with the following amended paragraph:

[0258] One embodiment of an upgradeable system is illustrated in **FIG. 28** and **FIG. 29**. The system of FIG. 28 illustrates a "Stand-Alone" embodiment, and includes an implantable housing 400 coupled to an implantable lead 402 with a connector 404. In one embodiment, the housing 400 is the housing 7 as described above. In another embodiment, the lead 402 is the lead

318 or lead 10 as described above. In one embodiment, connector 404 is the IS1 header 316, IS1 port 317, or connector 10, as described above. The connector 404 may be any connector known to those of skill in the art used to couple an implantable lead to an implantable housing.

Please replace paragraph **[0262]** with the following amended paragraph:

[0262] The housing 400 of the combination unit includes an antenna 408, battery 410, telemetry module 412, communication and power pulses module 414, programming module 416, and pacing circuitry 418. The battery 410 provides power to the components within the housing 410, as well as those within the sensor module (not shown), as describe above. The telemetry module 412 provides communication between the combination unit and the patient advisory module (not shown). The communication and power pulses module 414 control communication between the sensor module (not shown) and the housing 400 components as well as power distribution to the sensor module from the battery 410. Programming module 416 provides programming control over the system, including the pacing module 418, which controls the transmission of electrical pulses or stimuli as required by the CRM device.

Please replace paragraph **[0294]** with the following amended paragraph:

[0294] In one embodiment, data stored in the external patient advisory module is uploaded to the physician's PC at the time of the patient's regular office visit. The external device is placed in a data interface cradle connected to the PC, and the data is transferred. In one embodiment of the data transfer, the external device is a modified personal data assistant such as a PALM PILOT™ (Palm Computing, Inc.)~~Pilot~~, and the data interface cradle is the cradle used by such PDA devices for data synchronization with a personal computer.

Please replace paragraph **[0313]** with the following amended paragraph:

[0313] In one embodiment, the external device will further instruct the patient, using its graphical interface, to enter additional information relevant to the patient's condition, such as weight, peripheral blood pressure, and symptoms. The signal processing apparatus of the external device then compares the measured physiological parameters from the implanted device, together with information entered by the patient, with ranges and limits corresponding to

different therapeutic actions as predetermined by the physician and stored in the external device as a dynamic prescription or "DynamicRx™ (Savacor, Inc.)." The prescribed therapeutic action will then be communicated to the patient on the graphic display.

Please replace paragraph **[0315]** with the following amended paragraph:

[0315] As an example of a DynamicRx™ for a congestive heart failure patient, the level and rate of change of left atrial blood pressure (LAP) may be used by the physician to determine the dosage of diuretic. If the LAP remains in the normal range for that patient, the patient signaling device would display the normal dosage of diuretic. As in Example 1 above, if the LAP falls below the patient's normal range, the doctor may prescribe a reduction or withholding of diuretic, and that instruction would appear on the graphical interface. In another embodiment of DynamicRx™ the patient may be instructed to take some other kind of action, such as calling the physician or caregiver, altering diet or fluid intake, or getting additional rest. Thus, the apparatus and methods of the present invention allow the physician to conditionally prescribe therapy for the patient, and to communicate the appropriate therapy to the patient in response to dynamic changes in the patient's medical condition.

Please replace paragraph **[0316]** with the following amended paragraph:

[0316] In one embodiment, the physician enters the therapeutic plan for the patient, e.g., the DynamicRx™, on a personal computer and the DynamicRx™ is then loaded from the PC into the patient advisory module. In one embodiment, the patient advisory module is a PDA using the PALM OS® (Palm Computing, Inc.), or like ~~PalmOS~~ operating system, and the DynamicRx™ is loaded from the physician's PC via the HOTSYNC® (Palm Computing, Inc.), or like ~~HotSync~~ facility of ~~PalmOS~~PALM OS®. Loading of the DynamicRx™ from the physician's PC could be performed in the physician's office, or could be performed over a telephone modem or via a computer network, such as the Internet.

Please replace paragraph **[0317]** with the following amended paragraph:

[0317] In one embodiment, DynamicRx™ software running on the PC contains treatment templates that assist the physician in creating a complete DynamicRx™, such that

appropriate therapies/actions are provided for all possible values of the patient's physiological parameters.

Please replace paragraph **[0318]** with the following amended paragraph:

[0318] In one embodiment of the present invention, the DynamicRx™~~X~~ includes a patient instruction. In one embodiment, the patient instruction may includes directions or instructions to take medications, instructions to call 911, instructions to rest; or instructions to call a physician or medical care provider. In another embodiment of the present invention, one or more devices are provided to enable a physician or medical care provider to provide instruction to the patient. These devices include, but are not limited to, workstations, templates, PC-to-Palm hotsync operations, uploading processes, downloading processes, linking devices, wireless connections, networking, data cards, memory cards, and interface devices that permit the physician instruction to be loaded onto a patient's signal processor. In another embodiment, a user instruction is provided, where the user includes a patient, a physician, or a third party.